

an endothelial dependent vasodilator. Finally, 10 mM sodiumnitrite (an endothelial independent vasodilator) was added.

The patient group consisted of 37 patients, with a mean age of 61.4 (± 8.4) years, 27% was female and the mean dilation to ME was 40% ($\pm 24\%$) of the precontraction to PE. Linear regression showed that both total serum cholesterol (regression coefficient (r.c.) = 10.7%/mmol, $p = 0.008$) and LDL-cholesterol (r.c. = 11.5%/mmol, $p = 0.01$) were predictors for impaired endothelial dependent dilation. Adjusted for several other clinical characteristics in a multiple linear regression model, total serum cholesterol was the only statistically significant predictor of endothelial dysfunction (r.c. 10.6%/mmol, $p = 0.006$). Endothelial independent vasodilation to sodiumnitrite was not influenced by serum lipid levels.

These results indicate that total cholesterol is the best predictor for endothelial dysfunction in IMA's of coronary bypass patients.

921-111 Plaque rupture in men is associated with high serum cholesterol

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The association between coronary plaque rupture and risk factors has not been fully explored. We prospectively examined 164 hearts from men dying unexpectedly; there were 44 sudden coronary deaths (SCD) with plaque rupture (age 48 ± 9), 53 SCD with stable plaque with or without healed myocardial infarction (age 53 ± 11), 16 SCD with eroded plaques (age 46 ± 9) and 51 non-coronary deaths (age 49 ± 10 years). Hearts were perfusion fixed at physiologic pressures and coronary arteries sectioned serially. All areas of cross sectional luminal narrowing $\geq 50\%$ were evaluated histologically for thrombi. Postmortem sera were evaluated for % glycosylated hemoglobin, thiocyanate as an indicator for cigarette smoking, total cholesterol (TC), and high density lipoprotein cholesterol (HDL-C). Mean TC/HDL was 8.5 ± 0.6 in SCD with plaque rupture, exceeding controls (5.0 ± 0.3 , $p < 0.0001$), SCD with stable plaque (5.5 ± 0.6 , $p < 0.0001$), and SCD with eroded plaque (5.0 ± 1.9 , $p = 0.002$). By logistic regression, TC/HDL-C was a predictor of plaque rupture independent of age, glycosylated hemoglobin, heart weight, smoking history, and hypertension ($p = 0.0008$, odds ratio 5.1). These data suggest that the reduced morbidity and mortality by cholesterol lowering in primary and secondary prevention is related to the stabilization of plaques with prevention of plaque rupture.

921-112 Soluble Cell Adhesion Molecules Are Regulated by Plasma Cholesterol in Familial Hypercholesterolemia

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How cholesterol (CH) lowering produces clinical benefits, besides the angiographic evidences, it is unknown. In our study on the effects of low density lipoproteins (LDL)-apheresis in patients with diet and drug resistant familial hypercholesterolemia (FH) we addressed the specific question if high plasma CH levels "per se" may adversely affect endothelium adhesiveness and if this phenomenon might be reversible.

We studied, in 8 FH patients, the acute and after 2 and 6 days effect of CH removal on plasma intercellular adhesion molecule 1 (sICAM1) and on endothelium leukocyte adhesion molecule 1 (sELAM1). Apolipoprotein B containing lipoproteins were selectively absorbed on column of dextran sulfate cellulose and during 3.5-4 hours a plasma volume of 6.5-9.2 litres was treated. CH, CH-LDL, apo B, TG and Lp(a), were reduced by 74%, 82%, 79%, 56%, 86%, respectively. No significant effect was observed on HDL-CH. Clinical chemical and biocompatibility showed minimal changes. Basal sICAM1 and sELAM1 levels were higher compared to healthy control subjects; after, and not by, LDL-apheresis they were constantly and significantly ($p < 0.0001$ and $p < 0.0004$, respectively) reduced. Individual, pre and post treatment, values of both sICAM1 and sELAM1 were positively and significantly ($p < 0.0001$ and $p < 0.02$, respectively) correlated with total CH. Rebound sICAM1 and sELAM1 curves showed a pattern similar to that of total CH but not TG and Lp(a).

In the absence of changes of tumor necrosis factor and factors involved in inflammation, these results indicate a possible role for CH in regulating endothelium adhesiveness at least in FH and confirm, in a clinical setting, the upregulation of endothelium adhesiveness observed in atherogenesis induced in animal rendered hypercholesterolemics.

921-113 Influence of Hyperlipidemia on Restenosis After Coronary Artery Stent Implantation

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Restenosis after percutaneous coronary angioplasty (PTCA) depends on various mechanisms such as intimal hyperplasia, elastic recoil, arterial remodeling and smooth muscle proliferation, whereas restenosis after stent implantation is predominantly determined by neointimal proliferation. Hypercholesterolemia is known to be a major risk factor for coronary artery disease, but the association with neointimal proliferation has not been fully elucidated. Therefore, the role of lipids on the development of restenosis after stent placement has been investigated. We analyzed the association of serum lipids with the development of restenosis ($\geq 50\%$ diameter stenosis) of 750 lesions in 671 consecutive patients. They underwent successful stent implantation between March 93 and March 96 and had repeat angiography after a median of 191 days. For quantitative analysis an automated and computer assisted edge detection method was used. Serum levels of total cholesterol, LDL, HDL and Lp(a) were obtained at the time of the intervention and follow-up angiogram. There was no significant correlation of late lumen loss (mean: 1.1 ± 0.03 mm) within the stented segments or % restenosis (28.9%) and the levels of total cholesterol, LDL, HDL and Lp(a), neither at the time of the intervention nor at repeat angiography.

921-114 Reduction of Plasma Lipid Peroxides during low Density Lipoprotein Immunapheresis

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Extracorporeal low density lipoprotein (LDL) elimination is frequently used today for the treatment of drug-resistant hypercholesterolaemic patients. One of the most specific apheresis methods, LDL-immunapheresis, was developed to selectively remove LDL and lipoprotein (a) [Lp(a)] from plasma. Since lipid peroxidation is one of the unwanted side effects of extracorporeal plasma treatments, we followed the oxidative status of patients treated with LDL-immunapheresis. For this purpose lipid hydroperoxides, the primary products of lipid peroxidation and thiobarbituric acid-reacting substances (TBARS), secondary products, were determined in 13 patients before, during and after LDL-immunapheresis. The amount of plasma volume treated per patient was 6164 ± 546 ml. Treatment led to a reduction of total cholesterol by $69 \pm 8\%$, of LDL-cholesterol by $78.6 \pm 7.3\%$, of HDL-cholesterol by $19.2 \pm 7.1\%$ and of triglycerides by $37.6 \pm 21\%$. Apolipoprotein-B, Lp(a) and apoA1 were reduced by $77.1 \pm 6.45\%$, $25 \pm 5.6\%$ and $76.4 \pm 10.3\%$, respectively. Before treatment, mean plasma concentration of lipid hydroperoxides was 22.6 ± 15.2 $\mu\text{mol/L}$, whereas following treatment plasma hydroperoxides were reduced to 6.9 ± 7.4 $\mu\text{mol/L}$. This reduction of $64.7 \pm 27\%$ was statistically highly significant ($p < 0.001$). A non-significant change of TBARS concentration from 0.30 ± 0.26 $\mu\text{mol/L}$ to 0.23 ± 0.13 $\mu\text{mol/L}$ was also observed. We conclude that LDL-immunapheresis is not only very effective in reducing LDL- and Lp(a)-cholesterol, but also has a beneficial effect on the oxidative status of the patients.

921-115 Altering Physician Behavior in Lipid Testing and Therapy: Results of a Housestaff Education Program

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Treatment of hypercholesterolemia for secondary prevention of cardiac events is now firmly established. Lipid levels remain valid for 24 hours after the onset of myocardial infarction (MI) and 1994 national guidelines recommend measurement of serum lipids in patients (pts) within 24 hours in order to identify those in need of therapy. We designed a housestaff education project to alter physician behavior in obtaining lipid levels and treating elevated LDL-cholesterol in pts with acute coronary syndromes. The intervention consisted of formal didactic sessions on lipid testing and twice-weekly reinforcement sessions on rounds by the medical chief resident, along with posted reminders in clinical areas. All pts with MI during the two month study period (12/95-1/96) were identified by an elevated creatine kinase level and elevated MB fraction. Lipid testing and therapy rates were compared to a historical control population ($n = 280$) admitted with acute coronary syndromes over a previous recent 12 month period. **Results:** We identified 134 pts with MI. In pts for whom data was available, 35% had a history of hyperlipidemia, of whom 48% were on therapy at admission. Seventy percent of study pts compared to 45% of controls ($p = 0.0001$) had lipid levels drawn at some point during admission; 25% vs. 15% ($p = 0.03$) had fasting panels by hospital

day 2. In 58 pts without known prior hyperlipidemia, 59% were tested during admission (vs. 53%, $p = \text{NS}$); and 17% (vs. 17%, $p = \text{NS}$) had fasting panels by hospital day 2. Of tested pts who met criteria for treatment ($n = 34$), 35% received therapy at discharge. **Conclusion:** An intensive physician education program can significantly improve compliance with current guidelines for lipid testing but therapy remains suboptimal.

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Hypertension: Clinical Issues

Sunday, March 16, 1997, 5:00 p.m.–7:00 p.m.
 Anaheim Convention Center, Hall E
 Presentation Hour: 5:00 p.m.–7:00 p.m.

922-149

Lunchables® Increase Blood Pressure in Dahl Rats

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Human populations ingesting more than 80 mEq Na/day (1 mEq Na/kg body wt) demonstrate an increase in blood pressure (BP) with age resulting in premature death and disability. Lunchables® (L), a snack marketed to children, contains 1780 mg sodium (77.4 mEq Na) which is 2.2 mEq Na/kg for a 35 kg child. The cumulative effects of L on BP in Dahl Salt Sensitive (S) Rats were tested by feeding *ad libitum* ground up food for 22 days beginning at 12 weeks of age to Dahl S rats initially raised on a 0.4% Na diet. Rats were separated into 3 diet groups (4 rats each). Low (0.4% Na): composed of low Na rat chow, Medium (0.75% Na): a ground up diet of items purchased to simulate a lower Na L, and High (1.5% Na): a ground up diet composed of L. After 22 days intraarterial BP was measured in conscious rats over 3 days. Data were analyzed (table) by repeated measures analysis of variance: * $p < 0.05$ vs Low Na.

Diet Na	MAP (mm Hg)	Heart Wt (gm)	Kidney Wt (gm)
Low	133 ± 4.2	1.20 ± 0.03	2.68 ± 0.10
Medium	146 ± 4.6*	1.35 ± 0.05*	2.92 ± 0.10
High	159 ± 3.8*	1.41 ± 0.02*	3.36 ± 0.19*

The children's snack, L, and even a diet with 50% less Na, increased blood pressure, and induced cardiac and renal hypertrophy in this salt sensitive genotype. A Na induced increase in BP in any salt sensitive phenotype will result in detrimental effects including cardiac hypertrophy and renal damage. Children and adults from salt sensitive families and ethnic groups, should avoid these and other high Na snacks. Warnings of the toxic effects of sodium in many people should be placed on these dangerous snacks.

922-150

Does Gender Influence Diuretic Induced Lipid Changes?

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The purpose of the study was to assess the effect of diuretic therapy on lipid changes in male and female patients with hypertension. Several studies have shown mild and transient increase in LDL-cholesterol and triglycerides (Trig) with diuretic therapy but mostly in hypertensive men. Data in female hypertensives is scarce. In this study 61 males (age = 55 ± 13 years) and 24 females (age = 59 ± 8 years) with essential hypertension were treated with hydrochlorothiazide (HCTZ; average dose 42.5 mg daily). Both groups were followed for 6 months (m) with comparable diastolic BP reduction. Lipid changes within groups from baseline to 3 m and 6 m, in mg/dL, were as follows:

	Males				Females			
	3m	p	6m	p	3m	p	6m	p
Chol	10 ± 21	0.002	6 ± 25	0.18	18 ± 27	0.02	19 ± 20	0.002
LDL	4 ± 19	0.2	1 ± 24	0.87	17 ± 27	0.01	21 ± 21	0.002
Trig	35 ± 69	0.001	27 ± 108	0.13	14 ± 69	0.40	5 ± 49	0.73
HDL	0.3 ± 9	0.82	0.2 ± 7	0.86	-1 ± 8	0.50	-3 ± 7	0.18

p = p value

Unlike males, in hypertensive females, LDL-cholesterol and total cholesterol levels were sustained higher than baseline after 6 months of HCTZ but triglycerides did not rise significantly at 3 or 6 months. In males triglycerides and total cholesterol rose significantly at 3 months but decreased at 6 months. HDL-cholesterol levels did not change in either group.

Conclusion: Lipid changes with diuretic therapy are more pronounced and longer lasting in hypertensive women as compared to hypertensive men.

922-151

Alterations of Left Ventricular Geometry and Function in Subjects with White Coat Hypertension

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The prevalence of white coat hypertension (WCHT) in the general population and its relationship to left ventricular hypertrophy (LVH) and alterations of LV function is still unclear. To investigate this issue, we studied 1677 subjects of a population based cohort (WHO MONICA-Projekt, Augsburg). Blood pressure readings were performed in a sitting position according to a standardized protocol both during a 60 minutes period of relaxed conversation and filling out questionnaires (BP-T, mean of second and third measurement by a technician) and after echocardiography (BP-MD, by a physician). Subjects were characterized as normotensive (NT; BP-T and BP-MD < 140/90 mmHg, $n = 849$), mildly hypertensive (MHT; BP-T > 140/90 and BP-MD < 160/95 mmHg, $n = 129$), white coat hypertensive (WCHT; BP-T < 140/90, BP-MD > 160/95 mmHg, $n = 160$), and hypertensive (HTN; antihypertensive medication or BP-T > 140/90 and BP-MD > 160/95 mmHg, $n = 538$). WCHT were younger (51 years) than MHT and HTN (55 and 61 years), however more obese (28 kg/m²) than NT and MHT (25 and 26.5 kg/m²; $p < 0.05$ each). Systolic meridional wallstress as well as the prevalence of LVH (Penn mass; g/m) were markedly increased in WCHT (75 dynes/cm²; LVH 32%) and HTN (76 dynes/cm²; LVH 57%) compared to NT (68 dynes/cm²; LVH 12%) and MHT (71 dynes/cm²; LVH 19%), $p < 0.05$ each. Systolic function was normal, however, Doppler diastolic filling parameters were markedly altered in WCHT, MHT, and HTN (IntE/A 1.9, 1.7, and 1.4; IVRT 79, 80, and 89 ms) compared to NT (IntE/A 2.3, IVRT 74 ms, $p < 0.05$). Finally, multivariate analysis revealed that WCHT was a predictor of increased LV mass independent of body mass index, sex, and age. However, an independent impact of WCHT on diastolic filling was not detected. Thus, in the general population a large group of subjects with normal blood pressure is at increased risk for LVH due to exaggerated blood pressure response to mild stress.

922-152

The Relative Value of Pharmacological Stress Echo and Exercise Stress Testing for Risk Stratification in Hypertensives

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To assess the relative prognostic value of dipyridamole-atropine stress echo (DASE) (0.84 mg/kg over 10' + atropine up to 1 mg during 2-D echo and 12-lead ECG monitoring) and bicycle exercise electrocardiography testing (EET) (incremental workloads of 25 W every 2') in hypertension, the two tests were performed in 169 hypertensive patients (pts) (age 61 ± 8 years; mean \pm SD) with known or suspected coronary artery disease. No patient had a left bundle branch block at baseline ECG, was taking digitalis or antiarrhythmic medications. The only criterion for DASE positivity was the appearance of new functional abnormalities during test. ECG criterion of positivity during EET was an ST-segment shift ≥ 0.1 mV from baseline 80 msec after the J point in at least two contiguous leads. DASE was positive in 46 pts. EET was positive in 61 pts, 29 of whom had also a DASE positivity. During the follow-up (31 \pm 18 months) 36 cardiac events occurred: 3 deaths, 4 nonfatal infarctions, 10 unstable angina and 19 coronary revascularizations. The positive predictive value was higher for DASE compared with EET (54 vs. 35%; $p \leq 0.05$). It rose to 69% in pts having both DASE and EET positivity. The negative predictive value was 91% for DASE and 87% for EET ($p = \text{NS}$).

Pharmacological stress echo is more efficient than exercise electrocardiography testing for diagnostic purposes in hypertensives, but to date their relative prognostic values remain unknown. Our results show that DASE is more efficient than EET in risk stratification of hypertensives. However, a simple negative EET is sufficient to identify a very low risk subset in whom additional testing may not be warranted.

922-153

Inadequate High Blood Pressure Awareness and Control Using National Treatment Guidelines in a Population With Multiple Risk Factors

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The NIH National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC IV and V) Guidelines have been widely disseminated to physicians since 1988, supplemented with public education via the National High Blood Pressure Education Program. To determine the extent to which these guidelines were implemented in a high risk population of families with premature CHD, we examined the prevalence of hypertension (HTN) and